

REMARKS/ARGUMENTS

This amendment is in response to the final Official Action mailed on March 24, 2008. Entry of the foregoing and favorable reconsideration and reexamination of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.116, and in light of the remarks which follow, are respectfully requested.

By way of this response, claim 1 is amended, claim 4 is pending, claims 2, 3, and 5-31 are cancelled, and claims 32-39 are new. Support for amended claim 1 and new claims 38 and 39 can be found at ¶ [0030] of the pending application and original claims 5 and 10. New claims 32-37 are supported by original claims 13-20 and by ¶¶ [0028]-[0033]. For consistency, all paragraph references are to the published application, i.e. U.S. 2005/0101621. The fact that a particular passage supports a limitation should not be construed as an indication that support for that limitation can only be found or derived from that passage.

The Examiner has rejected claims 1 and 31 under 35 U.S.C. § 102(b) as allegedly anticipated by *Fink* (1972 Publication). Specifically, the Examiner states that "*Fink* teaches that using heroin challenges as his index, *Fink* observed complete blockade of heroin by intravenous administration of 1.0mg of naloxone" and complete blockade to heroin for 24 hours after a single oral dosage of 3.0gm. *Office Action*, pages 2-3. *emphasis added*. Applicant respectfully traverses these rejections.

*Fink* teaches single intravenous administrations of naloxone in amounts not to exceed 1.0mg. In contrast, amended claim 1 requires that a specific amount of naloxone, namely 50mg, be administered to the patient in a single dose. The amount administered according to claim 1 is therefore

significantly greater than the 1.0mg amount recited by *Fink*. Moreover, *Fink* only teaches administration of larger single doses in conjunction with oral administration and not via injection or infusion. Accordingly, amended claim 1 is not anticipated by *Fink* and the rejection should be withdrawn.

The Examiner has also rejected claims 1 and 5 under 35 U.S.C. § 103(a) as allegedly unpatentable over *McDonald* (April 2001 publication) in view of *Fink*. The Examiner believes it "would have been obvious to one of ordinary skill in the art at the time the invention was made to administer naloxone in [the] divide[d] daily dosages of 50mg taught by *McDonald* in a single dose...because *Fink* teaches that the naloxone can be administered in acute single intravenous doses." *Office Action*, pages 3-4. Moreover, the Examiner contends that there would be have been a reasonable expectation of success to deliver 50mg of naloxone in a single dosage because "the effectiveness of 50mg daily dosages of naloxone in treatment of opioid[] detoxification is well taught by *McDonald* and the effects of naloxone given in acute single intravenous diseases is well taught by *Fink*." *Id.* at page 4. Applicant respectfully disagrees.

Contrary to the Examiner's assertion, one skilled in the art would not have thought it obvious, regardless of the teachings of the cumulative art, to administer such high dosages of naloxone, especially in a single bolus injection.

First, an injection is not an infusion. Unlike the single bolus administration of a substance which characterizes an injection, one skilled in the art would recognize that an infusion is a continuous and slow introduction of a substance. Certainly, one skilled in the art would recognize the differences between injections and infusions and the effects they have on the administration of pharmaceuticals such as naloxone. *McDonald* exemplifies this distinction by teaching

infusions of 50mg of naloxone over a 24 hour period, with 25mg of naloxone infused over the first 30 minutes, and a supplemental 1mg infused over an hour for each hour thereafter. As shown in the table below, the infusion rates of *McDonald* are 0.83mg/min for the initial naloxone dose and significantly less, 0.01667mg/min, for each of the supplemental doses.

REFERENCE	ROUTE/AMOUNT
Claimed invention	Single injection 50mg
<i>McDonald</i> , initial	Infusion 25mg over 30min (0.83mg/min)
<i>McDonald</i> , supplemental	Infusion 1mg/hour (0.01667mg/min)
<i>Fink</i>	Single injection 1mg

In contrast, the doses of the claimed invention and *Fink* are not continuous, but are rather single bolus injections. Assuming *arguendo* that an injection is given over the duration of a minute, it is clear that *Fink*'s 1mg administration is similar to the initial infusion disclosed by *McDonald*, i.e. about 1mg/min. There is simply no disclosure in any of the cited references to deliver significantly higher amounts of naloxone over the short time period in which an injection is given and certainly no indication to delivery 50 times the dosage in a single bolus injection. Accordingly, one skilled in the art would not believe it obvious to administer 50mg of naloxone in a single dosage.

Moreover, while *McDonald* does teach the effectiveness of a 50mg dose of naloxone, *McDonald* only teaches this effectiveness over a sustained 24-hour administration. There is no indication in the cumulative art, however, that a 50mg dose or a 1.4mg/kg dose given in a single injection would have the same effectiveness or be able to provide the requisite opioid

detoxification. Nor is there any indication in any of the cited references that it would be safe to administer the claimed dosage (50mg or a dose according to weight of the patient at 1.4mg/kg) in such a short amount of time. Accordingly, one skilled in the art would not find it obvious to apply the administration methods of *Fink* with the dosage levels of *McDonald* especially when there is no indication that such a dosage administration would provide predictable and efficacious, not to mention safe, results. Therefore, the rejection of claim 1 should be withdrawn.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

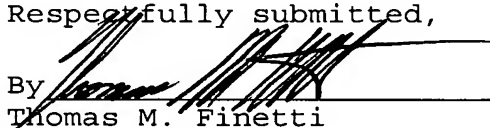
If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that she telephone applicant's attorney at (908) 654-5000 in order to overcome any additional objections which she might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Dated: June 24, 2008

Respectfully submitted,

By

  
Thomas M. Finetti

Registration No.: 61,881  
LERNER, DAVID, LITTENBERG,  
KRUMHOLZ & MENTLIK, LLP  
600 South Avenue West  
Westfield, New Jersey 07090  
(908) 654-5000  
Attorney for Applicant